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=> file caplus
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L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
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=> s l7 and (seh or epoxide hydrolase)
           663 SEH
            10 SEHS
           663 SEH
                 (SEH OR SEHS)
         52008 EPOXIDE
         30226 EPOXIDES
         67936 EPOXIDE
                 (EPOXIDE OR EPOXIDES)
         24872 HYDROLASE
          9348 HYDROLASES
         29509 HYDROLASE
                 (HYDROLASE OR HYDROLASES)
          2959 EPOXIDE HYDROLASE
                 (EPOXIDE(W)HYDROLASE)
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=> d his

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L2            1 S JP07304755/PN
L3            0 S 5962455/PN
L4            1 S US5962455/PN
                SELECT L2 1 RN
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L5        74206 S E1-E117
L6           28 S L5 AND (SEH OR EPOXIDE HYDROLASE)
                SELECT L4 1 RN
L7        80303 S E1-E135
L8           31 S L7 AND (SEH OR EPOXIDE HYDROLASE)

=> focus l6 or l8
OR IS NOT VALID HERE
The term is either unrecognized or invalid.

=> foluc l6
FOLUC IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> folcu l6
FOLCU IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> focus l6
PROCESSING COMPLETED FOR L6
L9           28 FOCUS L6 1-

=> focus l8
PROCESSING COMPLETED FOR L8
L10          31 FOCUS L8 1-

=> d ibib abs hitstr 1-28 19

L9   ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:        2006:386356  CAPLUS
DOCUMENT NUMBER:         144:427964
TITLE:                   Multiple pharmacophore-containing inhibitors for
                         soluble epoxide hydrolase and
                         disease treatment
INVENTOR(S):             Hammock, Bruce D.; Kim, In-Hae; Morisseau, Christophe;
                         Watanabe, Takaho; Newman, John W.
PATENT ASSIGNEE(S):      The Regents of the University of California, USA
SOURCE:                  PCT Int. Appl., 179 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     WO 2006045119        A2    20060427    WO 2005-US38282        20051020
     WO 2006045119        A9    20060526
     WO 2006045119        A3    20070208
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
             NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
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AU 2005295167	A1	20060427	AU 2005-295167	20051020
CA 2584342	A1	20060427	CA 2005-2584342	20051020
US 20060270609	A1	20061130	US 2005-256685	20051020
EP 1814875	A2	20070808	EP 2005-817420	20051020

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

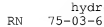
CN 101084216	A	20071205	CN 2005-80043035	20051020
JP 2008517072	T	20080522	JP 2007-538151	20051020
IN 2007KN01641	A	20070817	IN 2007-KN1641	20070508
PRIORITY APPLN. INFO.:			US 2004-651487P P	20041020
			WO 2005-US38282 W	20051020

OTHER SOURCE(S): MARPAT 144:427964

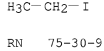
AB Inhibitors of the soluble epoxide hydrolase (sEH) are provided that incorporate multiple pharmacophores and are useful in the treatment of diseases such as hypertension and inflammation. Thus, hundreds of inhibitors were synthesized and tested as inhibitors of human and mouse sEH. The pharmacokinetics of various inhibitors was also studied.

IT 75-03-6, Ethyl iodide 75-30-9, Isopropyl iodide 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(multiple pharmacophore-containing inhibitors for soluble epoxide hydrolase and disease treatment)

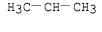
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)



RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)



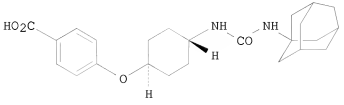
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



L9 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2007:764736 CAPLUS
DOCUMENT NUMBER:	147:343722
TITLE:	Orally Bioavailable Potent Soluble Epoxide Hydrolase Inhibitors
AUTHOR(S):	Hwang, Sung Hee; Tsai, Hsing-Ju; Liu, Jun-Yan; Morisseau, Christophe; Hammock, Bruce D.
CORPORATE SOURCE:	Department of Entomology and UCD Cancer Center, University of California, Davis, CA, 95616-8584, USA

SOURCE: Journal of Medicinal Chemistry (2007), 50(16), 3825-3840
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:343722
GI



I

AB A series of N,N'-disubstituted ureas having a conformationally restricted cis- or trans-1,4-cyclohexane α to the urea were prepared and tested as soluble epoxide hydrolase (sEH) inhibitors. This series of compds. showed low nanomolar to picomolar activities against recombinant human sEH. Both isomers showed similar potencies, but the trans isomers were more metabolically stable in human hepatic microsomes. Furthermore, these new potent inhibitors show a greater metabolic stability in vivo than previously described sEH inhibitors. Trans-4-[4-(3-adamantan-1-ylureido)cyclohexyloxy]benzoic acid (I, t-AUCB, IC50 = 1.3 ± 0.05 nM) had excellent oral bioavailability (98%, n = 2) and blood area under the curve in dogs and was effective in vivo to treat hypotension in lipopolysaccharide challenged murine models.
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cis and trans isomers of (adamantanylureido)cyclohexanol derivs. as orally bioavailable potent soluble epoxide hydrolase inhibitors)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph—CH_2—Br

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:644048 CAPLUS
DOCUMENT NUMBER: 147:72748
TITLE: Substituted pyrazole compounds useful as soluble epoxide hydrolase inhibitors and their preparation and pharmaceutical compositions
INVENTOR(S): Fleck, Roman Wolfgang; Guo, Xin; Lo, Ho Yin; Man, Chuk Chui
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 317pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007067836	A2	20070614	WO 2006-US60863	20061114
WO 2007067836	A3	20071115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

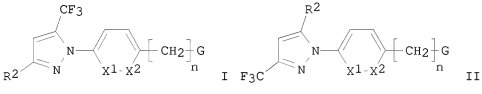
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

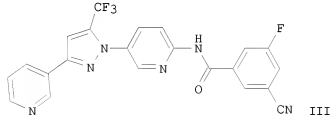
EP 1960367	A2	20080827	EP 2006-839868	20061114

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.:	US 2005-742350P	P	20051205
	WO 2006-US60863	W	20061114

OTHER SOURCE(S): MARPAT 147:72748
GI





AB Disclosed are compds. of formula I and II that are active against soluble epoxide hydrolase (sEH), compns. thereof and methods of using and making same. Compds. of formula I and II where G is acylamino; X1-X2 s CH=CH, N=CH, C=N, and N=N; R2 is (un)substituted heteroaryl and (un)substituted carbocycles; n is 0 - 5; and their pharmaceutically acceptable salts thereof, are claimed. Example compound III was prepared by acylation of 3-acetylpyridine with Et trifluoroacetate; the resulting 4,4,4-trifluoro-1-(pyridin-3-yl)butane-1,3-dione underwent cyclization with 2-fluoro-5-hydrazinopyridine to give 2-(6-fluoropyridin-3-yl)-5-(pyridin-3-yl)-3-trifluoromethyl-3,4-dihydro-2H-pyrazol-3-ol, which

underwent amination and elimination to give 5-(3-(pyridin-3-yl)-5-trifluoromethylpyrazol-1-yl)pyridin-2-ylamine, which underwent amidation with 3-cyano-5-fluorobenzoic acid to give compound III. All the invention compds. were evaluated for their sEH inhibitory activity.

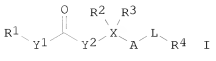
IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted pyrazole compds. useful as soluble epoxide hydrolase inhibitors)

RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)

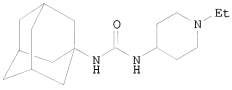
L9 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1061416 CAPLUS
DOCUMENT NUMBER: 147:385844
TITLE: Preparation of heterocyclic urea derivatives particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases
INVENTOR(S): Hammock, Bruce D.; Jones, Paul D.; Morisseau, Christophe; Huang, Huazhang; Tsai, Hsing-Ju; Gless, Richard, Jr.
PATENT ASSIGNEE(S): The Regents of the University of California, USA; Arete Therapeutics
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106525	A1	20070920	WO 2007-US6412	20070313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20070225283	A1	20070927	US 2007-685674	20070313

PRIORITY APPLN. INFO.: US 2006-782172P P 20060313
OTHER SOURCE(S): MARPAT 147:385844
GI



I



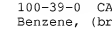
II

AB Title compds. I [R1 = (un)substituted alkyl, arylalkyl, cycloalkyl or heterocyclyl; Y1 = bond, C(R5)2, NR5 or O; Y2 = bond, NR5 and O; X = (CH2)n, wherein n = 0-1; R2, R3 and R5 independently = H, alkyl or COR6, wherein R6 = H, OH, NH2, alkyl or alkoxy; R4 = H, (un)substituted (hetero)alkyl, alkenyl, alkynyl, arylalkyl, cycloalkyl or heterocyclyl; A = (un)substituted heterocyclyl; L = direct bond, (hetero)alkylene, cycloalkylene, (hetero)arylene, CO, Se or SOm, wherein m = 0-2], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of soluble epoxide hydrolase (sEH). Thus, e.g., II was prepared by the reaction of 4-aminopiperidine with benzaldehyde and further protection with BOC-anhydride to provide intermediate carbamate which underwent acylation with 1-adamantyl isocyanate followed by deprotection and alkylation with bromoethane. I have an IC50 value against sEH of ≤ 150 nM. As inhibitors of sEH, I should prove useful for the treatment of hypertension, inflammation, adult respiratory distress syndrome, diabetic complications, end stage renal disease, Raynaud syndrome and arthritis. The invention also disclosed a cis-epoxyeicosantrienoic acid (EET) which can be administered with the sEH inhibitor (no data).

IT 100-39-0, Benzylbromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic urea derivs. particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:874483 CAPLUS

DOCUMENT NUMBER: 145:454915

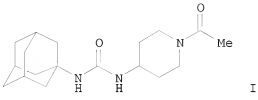
TITLE: Synthesis and SAR of conformationally restricted inhibitors of soluble epoxide hydrolase

AUTHOR(S): Jones, Paul D.; Tsai, Hsing-Ju; Do, Zung N.; Morisseau, Christophe; Hammock, Bruce D.

CORPORATE SOURCE: Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(19), 5212-5216

CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:454915
GI



I

AB A series of conformationally restricted inhibitors of human soluble epoxide hydrolase (sEH) was synthesized. Inhibition potency of the described compds. was studied against recombinant sEH. N-(1-Acetylpiperidin-4-yl)-N'-(adamant-1-yl) urea (I) was found to be a potent inhibitor that was also orally bioavailable in canines.

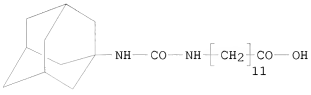
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, soluble epoxide hydrolase inhibiting activity, SAR and pharmacokinetics of (N-adamantyl-N'-piperidinyl)urea derivs. using alkylation and acylation of (N-adamantyl-N'-piperidinyl)urea hydrochloride as key steps)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1245497 CAPLUS
DOCUMENT NUMBER: 146:92622
TITLE: Design of bioavailable derivatives of 12-(3-adamantan-1-yl-ureido)dodecanoic acid, a potent inhibitor of the soluble epoxide hydrolase
AUTHOR(S): Kim, In-Hae; Nishi, Kosuke; Tsai, Hsing-Ju; Bradford, Tanya; Koda, Yasuko; Watanabe, Takaho; Morisseau, Christophe; Blanchfield, Joanne; Toth, Istvan; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and University of California Davis Cancer Center, University of California, Davis, CA, 95616, USA
SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1), 312-323
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:92622
GI

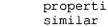


I

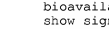
AB The soluble epoxide hydrolase (sEH) plays an important role in the metabolism of endogenous chemical mediators involved in blood pressure regulation and vascular inflammation. 12-(3-Adamantan-1-yl-ureido)-dodecanoic acid (AUDA, I) is a very active inhibitor of sEH both in vitro and in vivo. However, its relatively high m.p. and limited solubility in either water or oil-based solvents leads to difficulties in formulating the compound and often results in poor in vivo availability. We investigated the effect of derivatization of the acid functional group of inhibitor I on the inhibition potencies, phys. properties, and pharmacokinetic properties. For human sEH, similar inhibition potency was obtained when the acid of compound I was modified to esters. The resulting compds. exhibited improved phys. properties (23-66°C lower m.p. and 5-fold better solubility in oil). Pharmacokinetic studies showed that the esters possess improved oral bioavailability in mice. On the other hand, amide derivs. of I did not show significant improvement in inhibition potencies or phys. properties (higher m.ps. and lower solubility). The esterification of I results in compds. that are easier to formulate in animal food and in triglycerides for gavage and other routes of administration, making it easier to study the biol. effects of sEH inhibition in vivo.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(bioavailable derivs. of (adamantanylureido)dodecanoic acid as inhibitors of soluble epoxide hydrolase)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



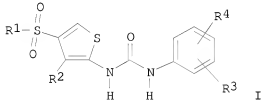
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:433827 CAPLUS
DOCUMENT NUMBER: 146:441658
TITLE: Preparation of 2-thienylurea derivatives as inhibitors of soluble epoxide hydrolase
INVENTOR(S): Takahashi, Hitomi; Ota, Tomomi; Kakinuma, Hiroyuki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043652	A1	20070419	WO 2006-JP320466	20061013

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-299465 A 20051013
OTHER SOURCE(S): MARPAT 146:441658
GI



I

AB The title compds. I [R1 = alkyl, cycloalkyl, etc.; R2 = H, halo, alkyl; R3, R4 = H, halo, alkyl, alkoxy, etc.] are prepared I are useful in the treatment of hypertension, etc. Thus, 1-[3-chloro-4-(isopropylsulfonyl)-2-thienyl]-3-[3-(trifluoromethyl)phenyl]urea was prepared in several steps from 3-amino-4-(isopropylsulfonyl)thiophene-2-carboxylic acid Et ester. Compds. of this invention showed IC50 values of 0.03 μM to 0.31 μM against soluble epoxide hydrolase.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-thienylurea derivs. as inhibitors of soluble epoxide hydrolase)

RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:465674 CAPLUS
DOCUMENT NUMBER: 125:161867
ORIGINAL REFERENCE NO.: 125:30167a,30170a
TITLE: Regioselectivity of Rhodococcus NCIMB 11216 epoxide hydrolase: applicability of E-values for description of enantioselectivity depends on substrate structure
AUTHOR(S): Mischitz, M.; Mirtl, C.; Saf, R.; Faber, K.
CORPORATE SOURCE: Inst. of Organic Chemistry, Graz Univ. of Technology, Graz, A-8010, Austria
SOURCE: Tetrahedron: Asymmetry (1996), 7(7), 2041-2046
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:161867
AB The regioselectivity of purified epoxide hydrolase from Rhodococcus NCIMB 11216 was investigated by hydrolyzing a series of structurally different epoxides 1a-5a in 18O-labeled water followed by GC/MS anal. of the 1,2-diols formed 1b-5b. The enzyme introduced a single 18O-atom in a trans-specific fashion with a varying degree of regioselectivity depending on the substitution pattern of the substrate. With an aliphatic mono-1a and 2,2-disubstituted oxirane 3a the attack occurred exclusively at the less hindered C-atom and complete retention of configuration was retained. The regioselectivity was low with a 2,3-di-4a and a trisubstituted epoxide 5a, and with a substrate bearing a benzylic oxirane atom 2a. As a consequence, the 'Enantiomeric Ratio' (E) can be applied to describe the selectivity of kinetic resolns. for some, but not for all types of substrates.
IT 75-03-6, Ethyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of epoxide hydrolase substrates and products)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

L9 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1015927 CAPLUS
TITLE: Epoxide Hydrolase Lsd19 for Polyether Formation in the Biosynthesis of Lasalocid A: Direct Experimental Evidence on Polyene-Polyepoxide Hypothesis in Polyether Biosynthesis
AUTHOR(S): Shichijo, Yoshihiro; Migita, Akira; Oguri, Hiroki; Watanabe, Mami; Tokiwano, Tetsuo; Watanabe, Kenji; Oikawa, Hideaki
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060-0810, Japan

SOURCE: Journal of the American Chemical Society ACS ASAP
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

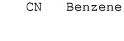
AB Polyether metabolites are an important class of natural products. Although their biosynthesis, especially construction of polyether skeletons, attracted organic chemists for many years, no exptl. data on the enzymic polyether formation has been obtained. In this study, a putative epoxide hydrolase gene lsd19 found on the biosynthetic gene cluster of an ionophore polyether lasalocid was cloned and successfully overexpressed in Escherichia coli. Using the purified Lsd19, a proposed substrate, bisepoxyprelasalocid, and its synthesized analog were successfully converted into lasalocid A and its derivative via a 6-endo-tet cyclization mode. On the other hand, treatment of the bisepoxide with trichloroacetic acid gave isolasalocid A via a 5-exo-tet cyclization mode. Therefore, the enzymic conversion observed in this study unambiguously showed that the bisepoxyprelasalocid is an intermediate of the lasalocid biosynthesis and that Lsd19 catalyzes the sequential cyclic ether formations involving an energetically disfavored 6-endo-tet cyclization. This is the first example of the enzymic epoxide-opening reactions leading to a polyether natural product.

IT INDEXING IN PROGRESS

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(epoxide hydrolase Lsd19 for polyether formation in biosynthesis of lasalocid A)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:370383 CAPLUS
DOCUMENT NUMBER: 148:489431
TITLE: Development of Metabolically Stable Inhibitors of Mammalian Microsomal Epoxide Hydrolase
AUTHOR(S): Morisseau, Christophe; Newman, John W.; Wheelock, Craig E.; Hill, Thomas, III; Morin, Dexter; Buckpitt, Alan R.; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology, U. C. Cancer Center, University of California, Davis, CA, 95616, USA
SOURCE: Chemical Research in Toxicology (2008), 21(4), 951-957
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The microsomal epoxide hydrolase (mEH) plays a significant role in the metabolism of xenobiotics such as polyarom. toxicants. Addnl., polymorphism studies have underlined a potential role of this enzyme in relation to a number of diseases, such as emphysema, spontaneous abortion, eclampsia, and several forms of cancer. We recently demonstrated that fatty amides, such as elaidamide, represent a new class of potent inhibitors of mEH. While these compds. are very active on recombinant mEH in vitro, they are quickly inactivated in liver exts.

reducing their value in vivo. We investigated the effect of structural changes on mEH inhibition potency and microsomal stability. Results obtained indicate that the presence of a small alkyl group α to the terminal amide function and a thio-ether β to this function increased mEH inhibition by an order of magnitude while significantly reducing microsomal inactivation. The addition of a hydroxyl group 9-10 carbons from the terminal amide function resulted in better inhibition potency without improving microsomal stability. The best compound obtained, 2-nonylsulfanyl-propionamide, is a competitive inhibitor of mEH with a KI of 72 nM. Furthermore, this new inhibitor significantly reduces mEH diol production in ex vivo lungs exposed to naphthalene, underlying the usefulness of the inhibitors described herein. These novel inhibitors could be valuable tools to investigate the physiol. and biol. roles of mEH.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(development of metabolically stable inhibitors of mammalian microsomal epoxide hydrolase)

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:525804 CAPLUS

DOCUMENT NUMBER: 147:157043

TITLE: The role of pharmacogenetics in the metabolism of antiepileptic drugs: pharmacokinetic and therapeutic implications

AUTHOR(S): Klotz, Ulrich

CORPORATE SOURCE: Dr Margarete Fischer-Bosch Institut fuer Klinische Pharmakologie, Stuttgart, Germany

SOURCE: Clinical Pharmacokinetics (2007), 46(4), 271-279
CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Wolters Kluwer Health

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

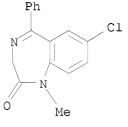
AB A review. Several different factors, including pharmacogenetics, contribute to inter-individual variability in drug response. Like most other agents, many antiepileptic drugs (AEDs) are metabolized by a variety of enzymic reactions, and the cytochrome P 450 (CYP) superfamily has attracted considerable attention. Some of those CYPs exist in the form of genetic (allelic) variants, which may also affect the plasma concns. or drug exposure (area under the plasma concentration-time curve [AUC]) of AEDs. With regard to the metabolism of AEDs, the polymorphic CYP2C9 and CYP2C19 are of interest. This review summarizes the evidence as to whether such polymorphisms affect the clin. action of AEDs. In the case of mephenytoin, defects in its metabolism may be attributable to >10 mutated alleles (designated as *2, *3 and others) of the gene expressing CYP2C19. Consequently, poor metabolizers (PMs) and extensive metabolizers (EMs) could be differentiated, whose frequencies vary among ethnic populations. CYP2C19 contributes to the metabolism of diazepam and phenytoin, the latter drug also representing a substrate of CYP2C9, with its predominant variants being defined as *2 and *3. For both AEDs, there is maximally a 2-fold difference in the hepatic elimination rate (e.g. clearance) or the

AUC between the extremes of EMs and PMs which, in the case of phenytoin (an AED with a narrow 'therapeutic window'), would suggest a dosage reduction only for patients who are carriers of mutated alleles of both CYP2C19 and CYP2C9, a subgroup that is very rare among Caucasians (about 1% of the population) but more frequent in Asians (about 10%). The minor contribution of CYP2C19 to the metabolism of phenobarbital (phenobarbitone) can be overlooked. In rare cases, valproic acid can be metabolized to the reactive (hepatotoxic) metabolite, 4-ene-valproic acid. It is not yet clear whether genetic variants of the involved enzyme (CYP2C9) are responsible for this problem. Likewise, the active metabolite of carbamazepine, carbamazepine-10,11-epoxide, is transformed by the microsomal epoxide hydrolase, an enzyme that is also highly polymorphic, but the pharmacokinetic and clin. consequences still need to be evaluated. Pharmacogenetic investigations have increased our general knowledge of drug disposition and action. As for old and especially new AEDs the pharmacogenetic influence on their metabolism is not very striking, it is not surprising that there are no treatment guidelines taking pharmacogenetic data into account. Therefore, the traditional and validated therapeutic drug monitoring approach, representing a direct 'phenotype' assessment, still remains the method of choice when an individualized dosing regimen is anticipated. Nevertheless, pharmacogenetics and pharmacogenomics can offer some novel contributions when attempts are made to maximize drug efficacy and enhance drug safety.

IT 439-14-5, Diazepam
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CYP2C9 gene influenced metabolism of diazepam in epileptic patient)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:393072 CAPLUS

DOCUMENT NUMBER: 137:216786

TITLE: Asymmetric total synthesis of (+)-exo-brevicomin based on enantioconvergent biocatalytic hydrolysis of an alkene-functionalized 2,3-disubstituted epoxide

AUTHOR(S): Mayer, Sandra F.; Mang, Harald; Steinreiber, Andreas; Saf, Robert; Faber, Kurt

CORPORATE SOURCE: Department of Chemistry, Organic & Bioorganic Chemistry, University of Graz, Graz, A-8010, Austria

SOURCE: Canadian Journal of Chemistry (2002), 80(4), 362-369
CODEN: CJCHAG; ISSN: 0008-4042

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

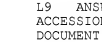
OTHER SOURCE(S): CASREACT 137:216786

AB A short total asym. synthesis of (+)-exo- and (-)-endo-brevicomin, which are components of the attracting pheromone system of several bark-beetle species belonging to the genera Dendroctonus and Dryocoetes, was accomplished via a chemoenzymic protocol. The key step consisted of biocatalytic hydrolysis by bacterial epoxide hydrolases of cis-configured 2,3-disubstituted oxiranes bearing olefinic side chains. This reaction proceeded in an enantioconvergent fashion, by affording a single enantiomeric vic-diol from the rac-epoxide in up to 92% ee and 83% isolated yield.

IT 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. total synthesis of (+)-exo-brevicomin based on enantioconvergent biocatalytic hydrolysis of alkene-functionalized 2,3-disubstituted epoxide)

RN 106-95-6 CAPLUS

CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:326455 CAPLUS

DOCUMENT NUMBER: 131:208530

TITLE: A multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicology

AUTHOR(S): de Sousa, Georges; Nicolas, Florence; Placidi, Michel; Rahmani, Roger; Benicourt, Marc; Vannier, Bernard; Lorenzon, Giocondo; Mertens, Karine; Coecke, Sandra; Callaerts, Andre; Rogiers, Vera; Khan, Shamas; Roberts, Phil; Skett, Paul; Fautrel, Alain; Chesne, Christophe; Guillouzo, Andre

CORPORATE SOURCE: INSERM/Centre de Recherche Agronomique, Antibes, 06606, Fr.

SOURCE: Chemico-Biological Interactions (1999), 121(1), 77-97
CODEN: CBINA8; ISSN: 0009-2797

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

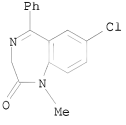
AB Ethical, economic and tech. reasons hinder regular supply of freshly isolated hepatocytes from higher mammals such as monkey for preclin. evaluation of drugs. Hence, the authors aimed at developing optimal and reproducible protocols to cryopreserve and thaw parenchymal liver cells from this major toxicol. species. Before the routine use of these protocols, the authors validated them through a multi-laboratory study. Dissociation of the whole animal liver resulted in obtaining 1-5 billion parenchymal cells with a viability of about 86%. An appropriate fraction (around 20%) of the freshly isolated cells was immediately set in primary culture and various hepato-specific tests were performed to examine their metabolic, biochem. and toxicol. functions as well as their ultrastructural characteristics. The major part of the hepatocytes was frozen and their functionality checked using the same parameters after thawing. The characterization of fresh and thawed monkey hepatocytes demonstrated the maintenance of various hepato-specific functions. Indeed, cryopreserved hepatocytes were able to survive and to function in culture as well as their fresh counterparts. The ability for synthesis (proteins, ATP, GSH) and conjugation and secretion of biliary acids was

preserved after deep freeze storage. A better stability of drug metabolizing activities than in rodent hepatocytes was observed in monkey. After thawing, Phase I and Phase II activities (cytochrome P 450, ethoxycoumarin-O-deethylase, aldrin epoxidase, epoxide hydrolase, glutathione transferase, glutathione reductase and glutathione peroxidase) were well preserved. The metabolic patterns of several drugs were qual. and quant. similar before and after cryopreservation. Lastly, cytotoxicity tests suggested that the freezing/thawing steps did not change cell sensitivity to toxic compds.

IT 439-14-5, Diazepam
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism; multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicol. in relation to drug metabolism)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:415295 CAPLUS

DOCUMENT NUMBER: 127:130797

ORIGINAL REFERENCE NO.: 127:25089a,25092a

TITLE: In vivo induction and in vitro inhibition of hepatic cytochrome P450 activity by the benzodiazepine anticonvulsants clonazepam and diazepam

AUTHOR(S): Nims, Raymond W.; Prough, Russell A.; Jones, Collins R.; Stockus, Diana L.; Dragnev, Konstantin H.; Thomas, Paul E.; Lubet, Ronald A.

CORPORATE SOURCE: Chemistry Section, Laboratory of Comparative Carcinogenesis and Biological Carcinogenesis and Development Program, National Cancer Inst., USA

SOURCE: Drug Metabolism and Disposition (1997), 25(6), 750-756
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

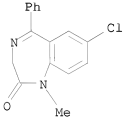
AB The ability of the benzodiazepines, as a chemical class, to cause the induction and/or inhibition of cytochromes P 450 has not been well characterized. In the present study, the induction of the cytochrome P 450 2B subfamily (CYP2B) in vivo and the inhibition of CYP2B activity in vitro by selected benzodiazepines was examined in hepatic tissues derived from male F344/NCr rats. Initial studies of the in vivo induction or in vitro inhibition of benzyloxyresorufin O-dealkylation activity revealed that both clonazepam and diazepam were relatively effective in vivo inducers of CYP2B when administered in the diet at 500 ppm for 5 days and also were fairly potent inhibitors of the activity of these hemoproteins in vitro. Oxazepam, in contrast, was ineffective as an inducer or an

inhibitor of this activity. Further studies were performed to characterize the subfamily selectivity of the P 450 induction and inhibition displayed by clonazepam. Specifically, microsomes from rats treated with clonazepam (1000 or 1800 ppm in the diet for 5 days) were found to be highly induced with respect to catalytic activities mediated by CYP2B, including benzyloxyresorufin and pentoxyresorufin O-dealkylation or testosterone 16β-hydroxylation, but other CYP proteins were minimally induced. In addition to inducing the CYP2B subfamily, clonazepam also induced the RNA encoding other drug metabolizing enzymes (e.g., epoxide hydrolase and the glutathione S-transferase α-subfamily) that are typically induced by phenobarbital-type inducers. Finally, clonazepam proved to be a potent noncompetitive or "mixed-type" competitive inhibitor of catalytic activities mediated by CYP2B, but not by other CYP proteins (e.g. CYP2A, CYP3A) in microsomes derived from phenobarbital-pretreated rats.

IT 439-14-5, Diazepam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(benzodiazepine anticonvulsants induction and inhibition of hepatic cytochrome P 450 activity)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



L9 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:407002 CAPLUS
Correction of: 2005:155217

DOCUMENT NUMBER: 143:248210
Correction of: 142:240243

TITLE: Product class 2: pyridinones and related systems

AUTHOR(S): Keller, P. A.

CORPORATE SOURCE: Germany

SOURCE: Science of Synthesis (2005), 15, 285-387
CODEN: SSCYJ9

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal; General Review

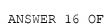
LANGUAGE: English

AB A review of methods to prepare pyridinones and related systems is presented. Synthetic methods include cyclization, aromatization, ring transformation, and substituent modification. The parent pyridinones are generally stable and are easily handled under standard laboratory conditions. The corresponding pyridinethiones are generally more reactive but have the advantage of generally requiring only standard laboratory equipment for their handling. The pyridineselenones are more reactive and the pyridinetellurones have not been comprehensively studied and characterized due to their reactivity and associated difficulty in production

IT 75-03-6 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridinones and related derivs. via cyclization,

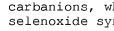
aromatization, ring transformation, and substituent modification)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



L9 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:767853 CAPLUS
DOCUMENT NUMBER: 141:410476
TITLE: Polystyrene-supported α-seleno carbanions: Efficient reagents for highly stereocontrolled syntheses of vinylphosphonates and vinyl sulfones
AUTHOR(S): Xu, Wei Ming; Tang, E.; Huang, Xian
CORPORATE SOURCE: Department of Chemistry, Zhejiang University, Hangzhou, 310028, Peop. Rep. China
SOURCE: Synthesis (2004), (13), 2094-2098
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:410476
AB Polystyrene-supported selenomethylphosphonate and polystyrene-supported selenomethyl sulfones have been prepared These novel reagents were treated with LDA or BuLi to produce polystyrene-supported α-seleno carbanions, which reacted with alkyl halides, followed by stereospecific selenoxide syn-elimination to give E-vinylphosphonates and E-vinyl sulfones resp. Also these novel polymer reagents can be regenerated and reused.
IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereocontrolled synthesis of vinylphosphonates and vinyl sulfones using polystyrene-supported selenomethylphosphonate and selenomethyl sulfone)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1977:189112 CAPLUS
DOCUMENT NUMBER: 86:189112
ORIGINAL REFERENCE NO.: 86:29653a,29656a
TITLE: The unsaturated esters of diselenophosphoric acid
AUTHOR(S): Zemlyanskii, N. L.; Mel'nik, Ya. G.; Turkevich, V. V.; Makota, I. P.; Koretskii, A. S.
CORPORATE SOURCE: USSR
SOURCE: Visnik L'vivs'kogo Derzhavnogo Universitetu, Seriya Khimichna (1975), 17, 65-8
CODEN: VLDUAB; ISSN: 0460-0509
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian
AB (RO)2P(Se)SeH (R = Et, Pr, Me2CH, Bu) were neutralized with K2CO3 and then treated with R1Br (R1 = allyl, HC.tplbond.CCH2) in Me2CO at 40° to give 71-82% (RO)2P(Se)SeR1 (I). Mol. association was deduced from the IR spectra of all 4 I (R1 = CH2C.tplbond.CH).
IT 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of dialkyl diselenophosphates with)
RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)

L9 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:455036 CAPLUS
DOCUMENT NUMBER: 121:55036
ORIGINAL REFERENCE NO.: 121:9891a
TITLE: Enhanced blood pressure response to mineralocorticoid stimulation in normotensive members of hypertensive families
AUTHOR(S): Ferrari, Paolo; Travaglini, Marco; Schild, Christoph; Allemann, Yves; Shaw, Sidney; Weidmann, Peter
CORPORATE SOURCE: Med. Poliklin., Univ. Berne, Switz.
SOURCE: Blood Pressure (1992), 1(2), 86-91
CODEN: BLPREG; ISSN: 0803-7051
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Currently normotensive offspring of essential hypertensive parents often have disturbances in blood pressure (BP) regulation such as abnormalities in electrolyte homeostasis, increased salt-sensitivity and/or impaired renal Na+-excretion. Whether an altered reactivity to mineralocorticoids may also play a role is presently unknown. Therefore, the authors investigated BP (recorded during 24 h), plasma atrial natriuretic factor (ANF), cyclic guanosine monophosphate (cGMP), aldosterone (PA) and renin activity (PRA), 24-h urine electrolyte and cGMP excretions measured on 4 consecutive days, as well as other variables, after 1 wk on placebo and after 3 wk of 9α-fludrocortisoneacetate (9αF) administration, 0.6 mg/d in 12 normotensive sons of essential hypertensive parents (SEH) and 12 body-mass-index- and age-matched (25±1[±SEM]yr) sons of normotensive parents (SN). On placebo, the 2 groups did not differ significantly in average 24 h BP (mean BP 95±2 mmHg), plasma-ANF (40±7 vs 30±5 pg/mL), cGMP (6±0.4 vs 6±0.5 nmol/L), PRA (1.3±0.1 vs 1.6±0.2 ng/mL/h), PA (9±0.5 vs 10±0.9 ng/dL), hematocrit (44±0.7 vs 44±0.4%) and 96-h urinary-Na+ (mean 205±13 vs 195±16 mmol/d), -K+ (69±6 vs 78±7 mmol/d) or -cGMP (461±35 vs 483±32 nmol/d). 9αF significantly increased BP in SEH

(p<0.005) but not SN (107±2 vs 100±2 mmHg, p<0.05). Elevation of BP during the night accounted for this difference (+13 vs +8 mmHg, p<0.02). However, during 9αF the 2 groups did not differ with regard of plasma ANF (106±13 vs 100±14 pg/mL), cGMP (10±1.1 vs 10±1.4 nmol/L), PRA (0.5±0.1 vs 0.5±0.2 ng/mL/h), PA (5±0.3 vs 4±0.3 ng/dL), 96-h urinary-Na+ (205±19 vs 195±17 mmol/d), -K+ (80±8 vs 69±6 mmol/d) or -cGMP (673±76 vs 653±62 nmol/d), plasma-Na+ (increase +3 vs +2 mmol/L), K+ (decrease -0.5 vs -0.5 mmol/L), hematocrit (42±0.8 vs 42±0.2%) or body weight (increase +2.0 vs +1.9 kg). These results indicate that normotensive offspring of hypertensive parents may react to mineralocorticoid stimulation with an enhanced BP-increase. This disturbance cannot be explained by insufficient renin-aldosterone suppression, inadequate ANF stimulation or abnormally increased Na+-fluid retention.

IT 9015-94-5, Renin, biological studies
RL: BIOL (Biological study)
(in plasma of normotensive sons from essential hypertensive families, enhanced blood pressure response to mineralocorticoid in relation to)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L9 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1938:63839 CAPLUS
DOCUMENT NUMBER: 32:63839
ORIGINAL REFERENCE NO.: 32:8937i,8938a
TITLE: Raman effect. LXXXVI. Ethyl derivatives
AUTHOR(S): Wagner, J.
SOURCE: Z. physik. Chem. (1938), B40, 439-49
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 32, 6549.5. Raman spectra were obtained for EtX, where X = OH, SH, Cl and I. Results of other investigations, where X = Me, NH2, Br and SeH have been included in the calcns. The mols. have been treated as a 3-particle system with a valence force potential energy function. The calculated vibrational frequencies agree with experiment only if the atomic weight of
X is less than 36. The valence force consts. are smaller and the nuclear distances are larger than those for the corresponding methyl derivs.
IT 75-03-6, Ethane, iodo-
(Raman spectrum of)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

L9 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1220997 CAPLUS
DOCUMENT NUMBER: 148:1283
TITLE: Estrogen receptor α is a major contributor to estrogen-mediated fetal testis dysgenesis and cryptorchidism
AUTHOR(S): Cederroth, Christopher R.; Schaad, Olivier; Descombes, Patrick; Chambon, Pierre; Vassalli, Jean-Dominique; Nef, Serge
CORPORATE SOURCE: Department of Genetic Medicine and Development, National Center of Competence in Research Frontiers in

Genetic, University of Geneva, Geneva, 1211/4, Switz.
SOURCE: Endocrinology (2007), 148(11), 5507-5519
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Failure of the testes to descend into the scrotum (cryptorchidism) is one of the most common birth defects in humans. In utero exposure to estrogens, such as 17β-estradiol (E2) or the synthetic estrogen diethylstilbestrol (DES), down-regulates insulin-like 3 (Insl3) expression in embryonic Leydig cells, which in turn results in cryptorchidism in mice. To identify the mol. mechanism whereby xenoestrogens block Insl3 gene transcription, we performed a microarray anal. of wild-type or estrogen receptor (ER) α-mutant testes exposed in utero to pharmacol. doses of E2 or DES. Six and 31 genes were resp. down-regulated and up-regulated by estrogen exposure (≥4-fold). All six genes down-regulated by estrogen exposure, including Insl3 and the steroidogenic genes steroidogenic acute regulatory protein and cytochrome P 450 17α-hydroxylase/17,20-lyase, were done so by an ERα-dependent mechanism. In contrast, up-regulation was mediated either by ERα for 12 genes or by an independent mechanism for the 19 remaining genes. Finally, we show that Insl3 gene expression and testicular descent were not affected by in utero exposure to E2 or DES in ERα mutant mice, whereas absence of ERβ did not influence the effect of these estrogens. Collectively, these data demonstrate that xenoestrogens inhibit the endocrine functions of fetal Leydig cells through an ERα-dependent mechanism.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen receptor α contribution to estrogen-mediated fetal testis dysgenesis and cryptorchidism)

RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:817105 CAPLUS
DOCUMENT NUMBER: 147:182868
TITLE: Use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances
INVENTOR(S): Mendrick, Donna L.; Johnson, Kory R.; Daniels, Kellye K.; Porter, Mark W.
PATENT ASSIGNEE(S): Gene Logic, Inc., USA
SOURCE: PCT Int. Appl., 203pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007084187	A2	20070726	WO 2006-US33712	20060828

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-711444P P 20050826

AB The present invention includes methods of predicting cardiotoxicity of test agents and methods of generating cardiotoxicity prediction models using algorithms for analyzing quant. gene expression information. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L9 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1248277 CAPLUS

DOCUMENT NUMBER: 146:22551

TITLE: Random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators

INVENTOR(S): Koltermann, Andre; Kettling, Ulrich; Haupts, Ulrich; Coco, Wayne; Tebbe, Jan; Votsmeier, Christian; Scheidig, Andreas

PATENT ASSIGNEE(S): Direvo Biotech AG, Germany

SOURCE: Eur. Pat. Appl., 93pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1726643	A1	20061129	EP 2005-104543	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20060269538	A1	20061130	US 2006-441635	20060526
WO 2006125827	A1	20061130	WO 2006-EP62644	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM
EP 1883696 A1 20080206 EP 2006-763303 20060526
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRIORITY APPLN. INFO.: EP 2005-104543 A 20050527
US 2005-685566P P 20050527
US 2005-686021P P 20050531
WO 2006-EP62644 W 20060526

AB The present invention provides a method for the selection of proteases with altered sensitivity to one or more activity-modulating substances. The method combines the provision of a protease library (i.e., phage display library) encoding polynucleotide sequences generated by using PCR mutagenesis, expression of the enzymes, screening of the library in the presence of one or several activity-modulating substances, selection of variants with altered sensitivity to one or several activity-modulating substances and isolation of those polynucleotide sequences that encode for the selected variants. In particular, mutant variants of human trypsin are disclosed.

IT 9015-94-5P, Renin, biological studies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators)

RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:712565 CAPLUS
DOCUMENT NUMBER: 138:470
TITLE: Failure of normal adult Leydig cell development in androgen-receptor-deficient mice
AUTHOR(S): O'Shaughnessy, Peter J.; Johnston, Heather; Willerton, Louise; Baker, Paul J.
CORPORATE SOURCE: Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow, G61 1QH, UK
SOURCE: Journal of Cell Science (2002), 115(17), 3491-3496
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During testicular development, fetal and adult populations of Leydig cells arise sequentially. Previous studies have shown that androgen action is required for normal steroidogenic activity in the mouse testis. Therefore, to determine the role of androgens in regulating fetal and adult Leydig cell differentiation and function, Leydig development has been measured in mice lacking functional androgen receptors (AR-null). The Leydig cell number was normal on day 5 after birth in AR-null mice but failed to increase normally thereafter and was about 30% of the control level on day 20 and about 60% of control level in adult animals. Levels of 15 different mRNA species expressed specifically in Leydig cells were measured by real-time PCR in AR-null and control animals. Expression levels of all mRNA species were normal on day 5 when only fetal Leydig cells are present. In older animals, which contain predominantly adult Leydig cells, five of the mRNA species (3β-hydroxysteroid dehydrogenase (3βHSD) type 1, cytochrome P 450scc, renin, StAR protein and luteinising hormone receptor) were expressed at normal or increased levels in AR-null mice. All other mRNA species measured showed

significantly reduced expression in older animals, and three of these mRNA species (17β-hydroxysteroid dehydrogenase type III, prostaglandin D (PGD)-synthetase and 3βHSD type VI), which are only expressed in the adult population of Leydig cells, were barely detectable in the adult AR-null mouse. The results show that in the absence of androgen receptors, fetal Leydig cell function is normal, but there is a developmental failure of adult Leydig cell maturation, with cells only acquiring partial characteristics of the adult population.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(androgen receptor role in regulating fetal and adult Leydig cell differentiation and function in development)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:929794 CAPLUS

DOCUMENT NUMBER: 137:89189

TITLE: Identification of novel peroxisome proliferator-activated receptor α (PPARα) target genes in mouse liver using cDNA microarray analysis

AUTHOR(S): Cherkaoui-Malki, Mustapha; Meyer, Kirstin; Cao, Wen-Qing; Latruffe, Norbert; Yeldandi, Anjana V.; Rao, M. Sambasiva; Bradfield, Christopher A.; Reddy, Janardan K.

CORPORATE SOURCE: Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611-3008, USA

SOURCE: Gene Expression (2001), 9(6), 291-304
CODEN: GEEXEJ; ISSN: 1052-2166

PUBLISHER: Cognizant Communication Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators, which function as peroxisome proliferator-activated receptor-α (PPARα) agonists, are a group of structurally diverse nongenotoxic hepatocarcinogens including the fibrate class of hypolipidemic drugs that induce peroxisome proliferation in liver parenchymal cells. Sustained activation of PPARα by these agents leads to the development of liver tumors in rats and mice. To understand the mol. mechanisms responsible for the pleiotropic effects of these agents, we have utilized the cDNA microarray to generate a mol. portrait of gene expression in the liver of mice treated for 2 wk with Wy-14,643, a potent peroxisome proliferator. PPARα activation resulted in the stimulation of expression (fourfold or greater) of 36 genes and decreased the expression (fourfold or more decrease) of 671 genes. Enhanced expression of several genes involved in lipid and glucose metabolism and many other genes associated with peroxisome biogenesis, cell surface function, transcription, cell cycle, and apoptosis has been observed These include: CYP2B9, CYP2B10, monoglyceride lipase, pyruvate dehydrogenase-kinase-4, cell death-inducing DNA-fragmentation factor-α, peroxisomal biogenesis factor 11β, as well as several cell recognition surface proteins including annexin A2, CD24, CD39, lymphocyte antigen 6, and retinoic acid early transcript-γ, among others. Northern blotting of total RNA extracted from the livers of PPARα-/- mice and from mice lacking both PPARα and peroxisomal fatty acyl-CoA oxidase (AOX), that were fed control and Wy-14,643-containing diets for 2 wk, as well as time course of induction following a single

dose of Wy-14,643, revealed that upregulation of genes identified by microarray procedure is dependent upon peroxisome proliferation vis-a-vis PPARα. However, cell death-inducing DNA-fragmentation factor-α mRNA, which is increased in the livers of wild-type mice treated with peroxisome proliferators, was not enhanced in AOX-/- mice with spontaneous peroxisome proliferation. These observations indicate that the activation of PPARα leads to increased and decreased expression of many genes not associated with peroxisomes, and that delayed onset of enhanced expression of some genes may be the result of metabolic events occurring secondary to PPARα activation and alterations in lipid metabolism

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identification of peroxisome proliferator-activated receptor α (PPARα) target genes in mouse liver using cDNA microarray anal.)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

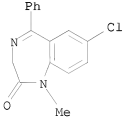
PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal

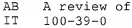
individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT 439-14-5, Diazepam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



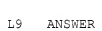
L9 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:991947 CAPLUS
DOCUMENT NUMBER: 149:245463
TITLE: Sodium Hydrogen Selenide
AUTHOR(S): Mlochowski, Jacek; Syper, Ludwik
CORPORATE SOURCE: Pol.
SOURCE: e-EROS Encyclopedia of Reagents for Organic Synthesis (2001), No pp. given. John Wiley & Sons, Inc.: Hoboken, N. J.
CODEN: 69KUHI
URL: http://www3.interscience.wiley.com/cgi-bin/mrwhome/104554785/HOME
DOCUMENT TYPE: Conference; General Review; (online computer file)
LANGUAGE: English
AB A review of the article Sodium Hydrogen Selenide.
IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Sodium Hydrogen Selenide)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



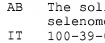
L9 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:358279 CAPLUS
Correction of: 2005:481371
DOCUMENT NUMBER: 145:123921

Correction of: 143:26021

TITLE: Acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogues
AUTHOR(S): Jung, K. W.; Nagle, A. S.
CORPORATE SOURCE: Dept. of Chemistry, University of South Florida, Tampa, FL, 33620-5250, USA
SOURCE: Science of Synthesis (2005), 18, 379-450
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review of the preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs.
IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



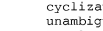
L9 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:495306 CAPLUS
DOCUMENT NUMBER: 144:128468
TITLE: Solid-phase synthesis of vinyl sulfones using polystyrene-supported selenomethyl phenyl sulfone
AUTHOR(S): Sheng, Shou Ri; Zhou, Wei; Liu, Xiao Ling; Xin, Qin; Song, Cai Sheng
CORPORATE SOURCE: Institutes of Chemistry, Jiangxi Normal University, Nanchang, 330027, Peop. Rep. China
SOURCE: Chinese Chemical Letters (2005), 16(5), 583-584
CODEN: CCLEE7; ISSN: 1001-8417
PUBLISHER: Chinese Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:128468
AB The solid-phase preparation of vinyl sulfones via a novel polystyrene-supported selenomethyl Ph sulfone reagent was reported.
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of vinyl sulfones by solid-phase reaction of chloromethylphenylsulfone with primary alkyl halides using polystyrene-supported selenium reagent)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr 1-31 18

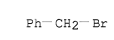
L8 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1015927 CAPLUS
TITLE: Epoxide Hydrolase Lsd19 for Polyether Formation in the Biosynthesis of Lasalocid A: Direct Experimental Evidence on Polyene-Polyepoxide Hypothesis in Polyether Biosynthesis
AUTHOR(S): Shichijo, Yoshihiro; Migita, Akira; Oguri, Hiroki; Watanabe, Mami; Tokiwano, Tetsuo; Watanabe, Kenji; Oikawa, Hideaki
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060-0810, Japan
SOURCE: Journal of the American Chemical Society ACS ASAP CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyether metabolites are an important class of natural products. Although their biosynthesis, especially construction of polyether skeletons, attracted organic chemists for many years, no exptl. data on the enzymic polyether formation has been obtained. In this study, a putative epoxide hydrolase gene lsd19 found on the biosynthetic gene cluster of an ionophore polyether lasalocid was cloned and successfully overexpressed in Escherichia coli. Using the purified Lsd19, a proposed substrate, bisepoxyprelasalocid, and its synthesized analog were successfully converted into lasalocid A and its derivative via a 6-endo-tet cyclization mode. On the other hand, treatment of the bisepoxide with trichloroacetic acid gave isolasalocid A via a 5-exo-tet cyclization mode. Therefore, the enzymic conversion observed in this study unambiguously showed that the bisepoxyprelasalocid is an intermediate of the lasalocid biosynthesis and that Lsd19 catalyzes the sequential cyclic ether formations involving an energetically disfavored 6-endo-tet cyclization. This is the first example of the enzymic epoxide-opening reactions leading to a polyether natural product.
IT INDEXING IN PROGRESS
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(epoxide hydrolase Lsd19 for polyether formation in biosynthesis of lasalocid A)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



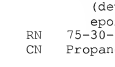
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:991947 CAPLUS
DOCUMENT NUMBER: 149:245463
TITLE: Sodium Hydrogen Selenide
AUTHOR(S): Mlochowski, Jacek; Syper, Ludwik
CORPORATE SOURCE: Pol.
SOURCE: e-EROS Encyclopedia of Reagents for Organic Synthesis (2001), No pp. given. John Wiley & Sons, Inc.: Hoboken, N. J.
CODEN: 69KUHI
URL: http://www3.interscience.wiley.com/cgi-bin/mrwhome/104554785/HOME
DOCUMENT TYPE: Conference; General Review; (online computer file)

LANGUAGE: English
AB A review of the article Sodium Hydrogen Selenide.
IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Sodium Hydrogen Selenide)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



L8 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:370383 CAPLUS
DOCUMENT NUMBER: 148:489431
TITLE: Development of Metabolically Stable Inhibitors of Mammalian Microsomal Epoxide Hydrolase
AUTHOR(S): Morisseau, Christophe; Newman, John W.; Wheelock, Craig E.; Hill, Thomas, III; Morin, Dexter; Buckpitt, Alan R.; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology, U. C. Cancer Center, University of California, Davis, CA, 95616, USA
SOURCE: Chemical Research in Toxicology (2008), 21(4), 951-957
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The microsomal epoxide hydrolase (mEH) plays a significant role in the metabolism of xenobiotics such as polyarom. toxicants. Addnl., polymorphism studies have underlined a potential role of this enzyme in relation to a number of diseases, such as emphysema, spontaneous abortion, eclampsia, and several forms of cancer. We recently demonstrated that fatty amides, such as elaidamide, represent a new class of potent inhibitors of mEH. While these compds. are very active on recombinant mEH in vitro, they are quickly inactivated in liver exts. reducing their value in vivo. We investigated the effect of structural changes on mEH inhibition potency and microsomal stability. Results obtained indicate that the presence of a small alkyl group α to the terminal amide function and a thio-ether β to this function increased mEH inhibition by an order of magnitude while significantly reducing microsomal inactivation. The addition of a hydroxyl group 9-10 carbons from the terminal amide function resulted in better inhibition potency without improving microsomal stability. The best compound obtained, 2-nonylsulfanyl-propionamide, is a competitive inhibitor of mEH with a KI of 72 nM. Furthermore, this new inhibitor significantly reduces mEH diol production in ex vivo lungs exposed to naphthalene, underlying the usefulness of the inhibitors described herein. These novel inhibitors could be valuable tools to investigate the physiol. and biol. roles of mEH.
IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(development of metabolically stable inhibitors of mammalian microsomal epoxide hydrolase)
RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1220997 CAPLUS
DOCUMENT NUMBER: 148:1283
TITLE: Estrogen receptor α is a major contributor to estrogen-mediated fetal testis dysgenesis and cryptorchidism
AUTHOR(S): Cederroth, Christopher R.; Schaad, Olivier; Descombes, Patrick; Chambon, Pierre; Vassalli, Jean-Dominique; Nef, Serge
CORPORATE SOURCE: Department of Genetic Medicine and Development, National Center of Competence in Research Frontiers in Genetic, University of Geneva, Geneva, 1211/4, Switz.
SOURCE: Endocrinology (2007), 148(11), 5507-5519
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Failure of the testes to descend into the scrotum (cryptorchidism) is one of the most common birth defects in humans. In utero exposure to estrogens, such as 17β-estradiol (E2) or the synthetic estrogen diethylstilbestrol (DES), down-regulates insulin-like 3 (Insl3) expression in embryonic Leydig cells, which in turn results in cryptorchidism in mice. To identify the mol. mechanism whereby xenoestrogens block Insl3 gene transcription, we performed a microarray anal. of wild-type or estrogen receptor (ER) α-mutant testes exposed in utero to pharmacol. doses of E2 or DES. Six and 31 genes were resp. down-regulated and up-regulated by estrogen exposure (≥4-fold). All six genes down-regulated by estrogen exposure, including Insl3 and the steroidogenic genes steroidogenic acute regulatory protein and cytochrome P 450 17α-hydroxylase/17,20-lyase, were done so by an ERα-dependent mechanism. In contrast, up-regulation was mediated either by ERα for 12 genes or by an independent mechanism for the 19 remaining genes. Finally, we show that Insl3 gene expression and testicular descent were not affected by in utero exposure to E2 or DES in ERα mutant mice, whereas absence of ERβ did not influence the effect of these estrogens. Collectively, these data demonstrate that xenoestrogens inhibit the endocrine functions of fetal Leydig cells through an ERα-dependent mechanism.
IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen receptor α contribution to estrogen-mediated fetal testis dysgenesis and cryptorchidism)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

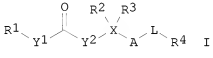
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1061416 CAPLUS
DOCUMENT NUMBER: 147:385844
TITLE: Preparation of heterocyclic urea derivatives particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases
INVENTOR(S): Hammock, Bruce D.; Jones, Paul D.; Morisseau,

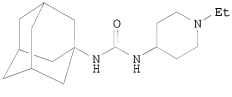
Christophe; Huang, Huazhang; Tsai, Hsing-Ju; Gless, Richard, Jr.
PATENT ASSIGNEE(S): The Regents of the University of California, USA; Arete Therapeutics
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106525	A1	20070920	WO 2007-US6412	20070313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20070225283	A1	20070927	US 2007-685674	20070313

PRIORITY APPLN. INFO.: US 2006-782172P P 20060313
OTHER SOURCE(S): MARPAT 147:385844
GI



I



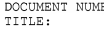
II

AB Title compds. I [R1 = (un)substituted alkyl, arylalkyl, cycloalkyl or heterocyclyl; Y1 = bond, C(R5)2, NR5 or O; Y2 = bond, NR5 and O; X = (CH2)n, wherein n = 0-1; R2, R3 and R5 independently = H, alkyl or COR6, wherein R6 = H, OH, NH2, alkyl or alkoxy; R4 = H, (un)substituted (hetero)alkyl, alkenyl, alkynyl, arylalkyl, cycloalkyl or heterocyclyl; A = (un)substituted heterocyclyl; L = direct bond, (hetero)alkylene, cycloalkylene, (hetero)arylene, CO, Se or SOm, wherein m = 0-2], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of soluble epoxide hydrolase (sEH). Thus, e.g., II was prepared by the reaction of 4-aminopiperidine with benzaldehyde and further protection with BOC-anhydride to provide intermediate carbamate which underwent acylation with 1-adamantyl isocyanate followed by deprotection and alkylation with bromoethane. I have an IC50 value against sEH of ≤ 150 nM. As inhibitors of sEH,

I should prove useful for the treatment of hypertension, inflammation, adult respiratory distress syndrome, diabetic complications, end stage renal disease, Raynaud syndrome and arthritis. The invention also disclosed a cis-epoxyeicosantrienoic acid (EET) which can be administered with the sEH inhibitor (no data).

IT 100-39-0, Benzylbromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic urea derivs. particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

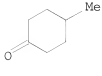
L8 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2007:1048489 CAPLUS
DOCUMENT NUMBER:	147:517065
TITLE:	Stereochemical preference of yeast epoxide hydrolase for the O-axial C3 epimers of 1-oxaspiro[2.5]octanes
AUTHOR(S):	Weijers, Carel A. G. M.; Koenst, Paul M.; Franssen, Maurice C. R.; Sudhoelter, Ernst J. R.
CORPORATE SOURCE:	Laboratory of Organic Chemistry, Wageningen University, Wageningen, 6703HB, Neth.
SOURCE:	Organic & Biomolecular Chemistry (2007), 5(19), 3106-3114 CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER:	Royal Society of Chemistry
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 147:517065

AB The 1-oxaspiro[2.5]octane moiety is a common motif in many biol. active spiroepoxide compds. Stereochem. plays an important role in the action of these spiroepoxides, since the O-axial C3 epimers are predominantly responsible for biol. activity. In view of this, the reactivity of the yeast epoxide hydrolase (YEH) from Rhodotorula glutinis towards both O-axial and O-equatorial C3 epimers of various 1-oxaspiro[2.5]octanes was investigated. O-axial C3 Epimers were hydrolyzed faster than the O-equatorial C3 epimers. The stereochem. preference was greatly dependent on the type of substitution on the cyclohexane ring. The preference of YEH for O-axial C3 epimers, found throughout this study, illustrates the effectiveness of YEH in enzymic detoxification of spiroepoxides.

IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereochem. preference of yeast epoxide hydrolase for O-axial C3 epimers of 1-oxaspiro[2.5]octanes)

RN 589-92-4 CAPLUS
CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:817105 CAPLUS
DOCUMENT NUMBER: 147:182868
TITLE: Use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances
INVENTOR(S): Mendrick, Donna L.; Johnson, Kory R.; Daniels, Kellye K.; Porter, Mark W.
PATENT ASSIGNEE(S): Gene Logic, Inc., USA
SOURCE: PCT Int. Appl., 203pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

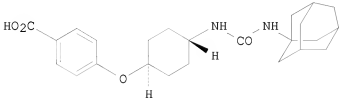
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007084187	A2	20070726	WO 2006-US33712	20060828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2005-711444P P 20050826
AB The present invention includes methods of predicting cardiotoxicity of test agents and methods of generating cardiotoxicity prediction models using algorithms for analyzing quant. gene expression information. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.
IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L8 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:764736 CAPLUS
DOCUMENT NUMBER: 147:343722
TITLE: Orally Bioavailable Potent Soluble Epoxide Hydrolase Inhibitors
AUTHOR(S): Hwang, Sung Hee; Tsai, Hsing-Ju; Liu, Jun-Yan; Morisseau, Christophe; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and UCD Cancer Center, University of California, Davis, CA, 95616-8584, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(16),

3825-3840
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:343722
GI



I

AB A series of N,N'-disubstituted ureas having a conformationally restricted cis- or trans-1,4-cyclohexane α to the urea were prepared and tested as soluble epoxide hydrolase (sEH) inhibitors. This series of compds. showed low nanomolar to picomolar activities against recombinant human sEH. Both isomers showed similar potencies, but the trans isomers were more metabolically stable in human hepatic microsomes. Furthermore, these new potent inhibitors show a greater metabolic stability in vivo than previously described sEH inhibitors. Trans-4-[4-(3-adamantan-1-ylureido)cyclohexyloxy]benzoic acid (I, t-AUCB, IC50 = 1.3 ± 0.05 nM) had excellent oral bioavailability (98%, n = 2) and blood area under the curve in dogs and was effective in vivo to treat hypotension in lipopolysaccharide challenged murine models.
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cis and trans isomers of (adamantanylureido)cyclohexanol derivs. as orally bioavailable potent soluble epoxide hydrolase inhibitors)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph—CH_2—Br

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:644048 CAPLUS
DOCUMENT NUMBER: 147:72748
TITLE: Substituted pyrazole compounds useful as soluble epoxide hydrolase inhibitors and their preparation and pharmaceutical compositions
INVENTOR(S): Fleck, Roman Wolfgang; Guo, Xin; Lo, Ho Yin; Man, Chuk Chui
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 317pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007067836	A2	20070614	WO 2006-US60863	20061114
WO 2007067836	A3	20071115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

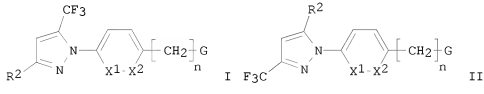
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

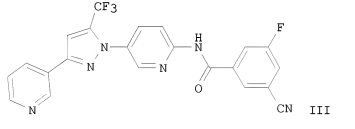
EP 1960367	A2	20080827	EP 2006-839868	20061114

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.:		US 2005-742350P	P 20051205
		WO 2006-US60863	W 20061114
OTHER SOURCE(S):	MARPAT 147:72748		

GI





AB Disclosed are compds. of formula I and II that are active against soluble epoxide hydrolase (sEH), compns. thereof and methods of using and making same. Compds. of formula I and II where G is acylamino; X1-X2 s CH=CH, N=CH, C=N, and N=N; R2 is (un)substituted heteroaryl and (un)substituted carbocycles; n is 0 - 5; and their pharmaceutically acceptable salts thereof, are claimed. Example compound III was prepared by acylation of 3-acetylpyridine with Et trifluoroacetate; the resulting 4,4,4-trifluoro-1-(pyridin-3-yl)butane-1,3-dione underwent cyclization with 2-fluoro-5-hydrazinopyridine to give 2-(6-fluoropyridin-3-yl)-5-(pyridin-3-yl)-3-trifluoromethyl-3,4-dihydro-2H-pyrazol-3-ol, which underwent amination and elimination to give 5-(3-(pyridin-3-yl)-5-trifluoromethylpyrazol-1-yl)pyridin-2-ylamine, which underwent amidation with 3-cyano-5-fluorobenzoic acid to give compound III. All the invention

compds. were evaluated for their sEH inhibitory activity.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted pyrazole compds. useful as soluble epoxide hydrolase inhibitors)

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)

L8 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:525804 CAPLUS

DOCUMENT NUMBER: 147:157043

TITLE: The role of pharmacogenetics in the metabolism of antiepileptic drugs: pharmacokinetic and therapeutic implications

AUTHOR(S): Klotz, Ulrich

CORPORATE SOURCE: Dr Margarete Fischer-Bosch Institut fuer Klinische Pharmakologie, Stuttgart, Germany

SOURCE: Clinical Pharmacokinetics (2007), 46(4), 271-279
CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Wolters Kluwer Health

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

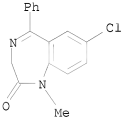
AB A review. Several different factors, including pharmacogenetics, contribute to inter-individual variability in drug response. Like most other agents, many antiepileptic drugs (AEDs) are metabolized by a variety of enzymic reactions, and the cytochrome P 450 (CYP) superfamily has attracted considerable attention. Some of those CYPs exist in the form of genetic (allelic) variants, which may also affect the plasma concns. or drug exposure (area under the plasma concentration-time curve [AUC]) of AEDs. With regard to the metabolism of AEDs, the polymorphic CYP2C9 and CYP2C19 are of interest. This review summarizes the evidence as to whether such polymorphisms affect the clin. action of AEDs. In the case of mephenytoin, defects in its metabolism may be attributable to >10 mutated alleles (designated as *2, *3 and others) of the gene expressing CYP2C19. Consequently, poor metabolizers (PMs) and extensive metabolizers (EMs) could be differentiated, whose frequencies vary among ethnic populations. CYP2C19 contributes to the metabolism of diazepam and phenytoin, the latter drug also representing a substrate of CYP2C9, with its predominant variants being defined as *2 and *3. For both AEDs, there is maximally a 2-fold difference in the hepatic elimination rate (e.g. clearance) or the AUC between the extremes of EMs and PMs which, in the case of phenytoin (an AED with a narrow 'therapeutic window'), would suggest a dosage reduction only for patients who are carriers of mutated alleles of both CYP2C19 and CYP2C9, a subgroup that is very rare among Caucasians (about 1% of the population) but more frequent in Asians (about 10%). The minor contribution of CYP2C19 to the metabolism of phenobarbital (phenobarbitone) can be overlooked. In rare cases, valproic acid can be metabolized to the reactive (hepatotoxic) metabolite, 4-ene-valproic acid. It is not yet clear whether genetic variants of the involved enzyme (CYP2C9) are responsible for this problem. Likewise, the active metabolite of carbamazepine, carbamazepine-10,11-epoxide, is transformed by the microsomal epoxide hydrolase, an enzyme that is also highly polymorphic, but the pharmacokinetic and clin. consequences still need to be evaluated. Pharmacogenetic investigations have increased our

general knowledge of drug disposition and action. As for old and especially new
AEDs the pharmacogenetic influence on their metabolism is not very striking, it is not surprising that there are no treatment guidelines taking pharmacogenetic data into account. Therefore, the traditional and validated therapeutic drug monitoring approach, representing a direct 'phenotype' assessment, still remains the method of choice when an individualized dosing regimen is anticipated. Nevertheless, pharmacogenetics and pharmacogenomics can offer some novel contributions when attempts are made to maximize drug efficacy and enhance drug safety.

IT 439-14-5, Diazepam
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CYP2C9 gene influenced metabolism of diazepam in epileptic patient)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

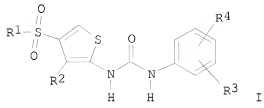
L8 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:433827 CAPLUS
DOCUMENT NUMBER: 146:441658
TITLE: Preparation of 2-thienylurea derivatives as inhibitors of soluble epoxide hydrolase
INVENTOR(S): Takahashi, Hitomi; Ota, Tomomi; Kakinuma, Hiroyuki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043652	A1	20070419	WO 2006-JP320466	20061013

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-299465 A 20051013
OTHER SOURCE(S): MARPAT 146:441658
GI

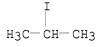


I

AB The title compds. I [R1 = alkyl, cycloalkyl, etc.; R2 = H, halo, alkyl; R3, R4 = H, halo, alkyl, alkoxy, etc.] are prepared I are useful in the treatment of hypertension, etc. Thus, 1-[3-chloro-4-(isopropylsulfonyl)-2-thienyl]-3-[3-(trifluoromethyl)phenyl]urea was prepared in several steps from 3-amino-4-(isopropylsulfonyl)thiophene-2-carboxylic acid Et ester. Compds. of this invention showed IC50 values of 0.03 μM to 0.31 μM against soluble epoxide hydrolase.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-thienylurea derivs. as inhibitors of soluble epoxide hydrolase)

RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1248277 CAPLUS
DOCUMENT NUMBER: 146:22551
TITLE: Random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators
INVENTOR(S): Koltermann, Andre; Kettling, Ulrich; Haupts, Ulrich; Coco, Wayne; Tebbe, Jan; Votsmeier, Christian; Scheidig, Andreas
PATENT ASSIGNEE(S): Direvo Biotech AG, Germany
SOURCE: Eur. Pat. Appl., 93pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1726643	A1	20061129	EP 2005-104543	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

US 20060269538 A1 20061130 US 2006-441635 20060526
WO 2006125827 A1 20061130 WO 2006-EP62644 20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
EP 1883696 A1 20080206 EP 2006-763303 20060526
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRIORITY APPLN. INFO.: EP 2005-104543 A 20050527
US 2005-685566P P 20050527
US 2005-686021P P 20050531
WO 2006-EP62644 W 20060526

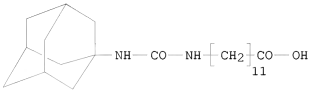
AB The present invention provides a method for the selection of proteases with altered sensitivity to one or more activity-modulating substances. The method combines the provision of a protease library (i.e., phage display library) encoding polynucleotide sequences generated by using PCR mutagenesis, expression of the enzymes, screening of the library in the presence of one or several activity-modulating substances, selection of variants with altered sensitivity to one or several activity-modulating substances and isolation of those polynucleotide sequences that encode for the selected variants. In particular, mutant variants of human trypsin are disclosed.

IT 9015-94-5P, Renin, biological studies
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1245497 CAPLUS
DOCUMENT NUMBER: 146:92622
TITLE: Design of bioavailable derivatives of 12-(3-adamantan-1-yl-ureido)dodecanoic acid, a potent inhibitor of the soluble epoxide hydrolase
AUTHOR(S): Kim, In-Hae; Nishi, Kosuke; Tsai, Hsing-Ju; Bradford, Tanya; Koda, Yasuko; Watanabe, Takaho; Morisseau, Christophe; Blanchfield, Joanne; Toth, Istvan; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and University of California Davis Cancer Center, University of California, Davis, CA, 95616, USA
SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1), 312-323
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:92622
GI

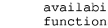


I

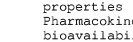
AB The soluble epoxide hydrolase (sEH) plays an important role in the metabolism of endogenous chemical mediators involved in blood pressure regulation and vascular inflammation. 12-(3-Adamantan-1-yl-ureido)-dodecanoic acid (AUDA, I) is a very active inhibitor of sEH both in vitro and in vivo. However, its relatively high m.p. and limited solubility in either water or oil-based solvents leads to difficulties in formulating the compound and often results in poor in vivo availability. We investigated the effect of derivatization of the acid functional group of inhibitor I on the inhibition potencies, phys. properties, and pharmacokinetic properties. For human sEH, similar inhibition potency was obtained when the acid of compound I was modified to esters. The resulting compds. exhibited improved phys. properties (23-66°C lower m.p. and 5-fold better solubility in oil). Pharmacokinetic studies showed that the esters possess improved oral bioavailability in mice. On the other hand, amide derivs. of I did not show significant improvement in inhibition potencies or phys. properties (higher m.ps. and lower solubility). The esterification of I results in compds. that are easier to formulate in animal food and in triglycerides for gavage and other routes of administration, making it easier to study the biol. effects of sEH inhibition in vivo.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(bioavailable derivs. of (adamantanylureido)dodecanoic acid as inhibitors of soluble epoxide hydrolase)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

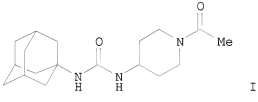


RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



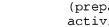
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:874483 CAPLUS
DOCUMENT NUMBER: 145:454915
TITLE: Synthesis and SAR of conformationally restricted inhibitors of soluble epoxide hydrolase
AUTHOR(S): Jones, Paul D.; Tsai, Hsing-Ju; Do, Zung N.; Morisseau, Christophe; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(19), 5212-5216
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:454915
GI



I

AB A series of conformationally restricted inhibitors of human soluble epoxide hydrolase (sEH) was synthesized. Inhibition potency of the described compds. was studied against recombinant sEH. N-(1-Acetylpiperidin-4-yl)-N'-(adamant-1-yl) urea (I) was found to be a potent inhibitor that was also orally bioavailable in canines.
IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, soluble epoxide hydrolase inhibiting activity, SAR and pharmacokinetics of (N-adamantyl-N'-piperidinyl)urea derivs. using alkylation and acylation of (N-adamantyl-N'-piperidinyl)urea hydrochloride as key steps)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:386356 CAPLUS
DOCUMENT NUMBER: 144:427964
TITLE: Multiple pharmacophore-containing inhibitors for

soluble epoxide hydrolase and disease treatment

INVENTOR(S): Hammock, Bruce D.; Kim, In-Hae; Morisseau, Christophe; Watanabe, Takaho; Newman, John W.

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006045119	A2	20060427	WO 2005-US38282	20051020
WO 2006045119	A9	20060526		
WO 2006045119	A3	20070208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005295167	A1	20060427	AU 2005-295167	20051020
CA 2584342	A1	20060427	CA 2005-2584342	20051020
US 20060270609	A1	20061130	US 2005-256685	20051020
EP 1814875	A2	20070808	EP 2005-817420	20051020
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101084216	A	20071205	CN 2005-80043035	20051020
JP 2008517072	T	20080522	JP 2007-538151	20051020
IN 2007KN01641	A	20070817	IN 2007-KN1641	20070508

PRIORITY APPLN. INFO.: US 2004-651487P P 20041020
WO 2005-US38282 W 20051020

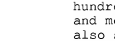
OTHER SOURCE(S): MARPAT 144:427964

AB Inhibitors of the soluble epoxide hydrolase (sEH) are provided that incorporate multiple pharmacophores and are useful in the treatment of diseases such as hypertension and inflammation. Thus, hundreds of inhibitors were synthesized and tested as inhibitors of human and mouse sEH. The pharmacokinetics of various inhibitors was also studied.

IT 75-03-6, Ethyl iodide 75-30-9, Isopropyl iodide
100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(multiple pharmacophore-containing inhibitors for soluble epoxide hydrolase and disease treatment)

RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)



RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

L8 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:358279 CAPLUS
Correction of: 2005:481371
DOCUMENT NUMBER: 145:123921
Correction of: 143:26021
TITLE: Acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogues
AUTHOR(S): Jung, K. W.; Nagle, A. S.
CORPORATE SOURCE: Dept. of Chemistry, University of South Florida, Tampa, FL, 33620-5250, USA
SOURCE: Science of Synthesis (2005), 18, 379-450
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review of the preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs.
IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

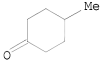
L8 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:621791 CAPLUS
DOCUMENT NUMBER: 143:286226
TITLE: Stereoselectivity and Substrate Specificity in the Kinetic Resolution of Methyl-Substituted 1-Oxaspiro[2.5]octanes by Rhodotorula glutinis Epoxide Hydrolase
AUTHOR(S): Weijers, Carel A. G. M.; Meeuwse, Petra; Herpers, Robert L. J. M.; Franssen, Maurice C. R.; Sudhoelter, Ernst J. R.
CORPORATE SOURCE: Laboratory of Organic Chemistry, Wageningen University, Wageningen, 6703HB W, Neth.
SOURCE: Journal of Organic Chemistry (2005), 70(17), 6639-6646
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:286226

AB The kinetic resolution of a range of methyl-substituted 1-oxaspiro[2.5]octanes by yeast epoxide hydrolase (YEH) from Rhodotorula glutinis has been investigated. The structural determinants of substrate specificity and stereoselectivity of YEH toward these substrates appeared to be the configuration of the epoxide ring and the substitution pattern of the cyclohexane ring. For all compds. tested, O-axial epoxides were hydrolyzed faster than the corresponding O-equatorial compds. In concern of the ring substituents, YEH preferred Me groups on the Re side of the ring. Placement of substituents close to the spiroepoxide carbon decreased the reaction rate but increased enantioselectivity. YEH-catalyzed kinetic resolution of 4-Me 1-oxaspiro[2.5]octane epimers were most enantioselective (E > 100).

IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfur ylide epoxidn.; stereoselectivity and substrate specificity in the kinetic resolution of methyl-substituted oxaspiro[2.5]octanes by Rhodotorula glutinis epoxide hydrolase)

RN 589-92-4 CAPLUS
CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



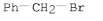
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:495306 CAPLUS
DOCUMENT NUMBER: 144:128468
TITLE: Solid-phase synthesis of vinyl sulfones using polystyrene-supported selenomethyl phenyl sulfone
AUTHOR(S): Sheng, Shou Ri; Zhou, Wei; Liu, Xiao Ling; Xin, Qin; Song, Cai Sheng
CORPORATE SOURCE: Institutes of Chemistry, Jiangxi Normal University, Nanchang, 330027, Peop. Rep. China
SOURCE: Chinese Chemical Letters (2005), 16(5), 583-584
CODEN: CCLEE7; ISSN: 1001-8417
PUBLISHER: Chinese Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:128468

AB The solid-phase preparation of vinyl sulfones via a novel polystyrene-supported selenomethyl Ph sulfone reagent was reported.

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of vinyl sulfones by solid-phase reaction of chloromethylphenylsulfone with primary alkyl halides using polystyrene-supported selenium reagent)

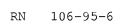
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:407002 CAPLUS
Correction of: 2005:155217
DOCUMENT NUMBER: 143:248210
Correction of: 142:240243
TITLE: Product class 2: pyridinones and related systems
AUTHOR(S): Keller, P. A.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2005), 15, 285-387
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review of methods to prepare pyridinones and related systems is presented. Synthetic methods include cyclization, aromatization, ring transformation, and substituent modification. The parent pyridinones are generally stable and are easily handled under standard laboratory conditions. The corresponding pyridinethiones are generally more reactive but have the advantage of generally requiring only standard laboratory equipment for their handling. The pyridineselenones are more reactive and the pyridinetellurones have not been comprehensively studied and characterized due to their reactivity and associated difficulty in production
IT 75-03-6 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridinones and related derivs. via cyclization, aromatization, ring transformation, and substituent modification)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



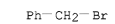
L8 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:767853 CAPLUS
DOCUMENT NUMBER: 141:410476
TITLE: Polystyrene-supported α-seleno carbanions: Efficient reagents for highly stereocontrolled syntheses of vinylphosphonates and vinyl sulfones
AUTHOR(S): Xu, Wei Ming; Tang, E.; Huang, Xian
CORPORATE SOURCE: Department of Chemistry, Zhejiang University, Hangzhou, 310028, Peop. Rep. China
SOURCE: Synthesis (2004), (13), 2094-2098
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:410476
AB Polystyrene-supported selenomethylphosphonate and polystyrene-supported selenomethyl sulfones have been prepared These novel reagents were treated

with LDA or BuLi to produce polystyrene-supported α-seleno carbanions, which reacted with alkyl halides, followed by stereospecific selenoxide syn-elimination to give E-vinylphosphonates and E-vinyl sulfones resp. Also these novel polymer reagents can be regenerated and reused.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereocontrolled synthesis of vinylphosphonates and vinyl sulfones using polystyrene-supported selenomethylphosphonate and selenomethyl sulfone)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:712565 CAPLUS
DOCUMENT NUMBER: 138:470
TITLE: Failure of normal adult Leydig cell development in androgen-receptor-deficient mice
AUTHOR(S): O'Shaughnessy, Peter J.; Johnston, Heather; Willerton, Louise; Baker, Paul J.
CORPORATE SOURCE: Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow, G61 1QH, UK
SOURCE: Journal of Cell Science (2002), 115(17), 3491-3496
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During testicular development, fetal and adult populations of Leydig cells arise sequentially. Previous studies have shown that androgen action is required for normal steroidogenic activity in the mouse testis. Therefore, to determine the role of androgens in regulating fetal and adult Leydig cell differentiation and function, Leydig development has been measured in mice lacking functional androgen receptors (AR-null). The Leydig cell number was normal on day 5 after birth in AR-null mice but failed to increase normally thereafter and was about 30% of the control level on day 20 and about 60% of control level in adult animals. Levels of 15 different mRNA species expressed specifically in Leydig cells were measured by real-time PCR in AR-null and control animals. Expression levels of all mRNA species were normal on day 5 when only fetal Leydig cells are present. In older animals, which contain predominantly adult Leydig cells, five of the mRNA species (3β-hydroxysteroid dehydrogenase (3βHSD) type 1, cytochrome P 450scc, renin, StAR protein and luteinising hormone receptor) were expressed at normal or increased levels in AR-null mice. All other mRNA species measured showed significantly reduced expression in older animals, and three of these mRNA species (17β-hydroxysteroid dehydrogenase type III, prostaglandin D

(PGD)-synthetase and 3βHSD type VI), which are only expressed in the adult population of Leydig cells, were barely detectable in the adult AR-null mouse. The results show that in the absence of androgen receptors, fetal Leydig cell function is normal, but there is a developmental failure of adult Leydig cell maturation, with cells only acquiring partial characteristics of the adult population.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(androgen receptor role in regulating fetal and adult Leydig cell differentiation and function in development)

RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

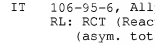
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:393072 CAPLUS
DOCUMENT NUMBER: 137:216786
TITLE: Asymmetric total synthesis of (+)-exo-brevicomin based on enantioconvergent biocatalytic hydrolysis of an alkene-functionalized 2,3-disubstituted epoxide
AUTHOR(S): Mayer, Sandra F.; Mang, Harald; Steinreiber, Andreas; Saf, Robert; Faber, Kurt
CORPORATE SOURCE: Department of Chemistry, Organic & Bioorganic Chemistry, University of Graz, Graz, A-8010, Austria
SOURCE: Canadian Journal of Chemistry (2002), 80(4), 362-369
CODEN: CJCHAG; ISSN: 0008-4042
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:216786

AB A short total asym. synthesis of (+)-exo- and (-)-endo-brevicomin, which are components of the attracting pheromone system of several bark-beetle species belonging to the genera Dendroctonus and Dryocoetes, was accomplished via a chemoenzymic protocol. The key step consisted of biocatalytic hydrolysis by bacterial epoxide hydrolases of cis-configured 2,3-disubstituted oxiranes bearing olefinic side chains. This reaction proceeded in an enantioconvergent fashion, by affording a single enantiomeric vic-diol from the rac-epoxide in up to 92% ee and 83% isolated yield.

IT 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. total synthesis of (+)-exo-brevicomin based on enantioconvergent biocatalytic hydrolysis of alkene-functionalized 2,3-disubstituted epoxide)

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:929794 CAPLUS
DOCUMENT NUMBER: 137:89189
TITLE: Identification of novel peroxisome

proliferator-activated receptor α (PPARα) target genes in mouse liver using cDNA microarray analysis

AUTHOR(S): Cherkaoui-Malki, Mustapha; Meyer, Kirstin; Cao, Wen-Qing; Latruffe, Norbert; Yeldandi, Anjana V.; Rao, M. Sambasiva; Bradfield, Christopher A.; Reddy, Janardan K.

CORPORATE SOURCE: Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611-3008, USA

SOURCE: Gene Expression (2001), 9(6), 291-304
CODEN: GEEXEJ; ISSN: 1052-2166

PUBLISHER: Cognizant Communication Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators, which function as peroxisome proliferator-activated receptor-α (PPARα) agonists, are a group of structurally diverse nongenotoxic hepatocarcinogens including the fibrate class of hypolipidemic drugs that induce peroxisome proliferation in liver parenchymal cells. Sustained activation of PPARα by these agents leads to the development of liver tumors in rats and mice. To understand the mol. mechanisms responsible for the pleiotropic effects of these agents, we have utilized the cDNA microarray to generate a mol. portrait of gene expression in the liver of mice treated for 2 wk with Wy-14,643, a potent peroxisome proliferator. PPARα activation resulted in the stimulation of expression (fourfold or greater) of 36 genes and decreased the expression (fourfold or more decrease) of 671 genes. Enhanced expression of several genes involved in lipid and glucose metabolism and many other genes associated with peroxisome biogenesis, cell surface function, transcription, cell cycle, and apoptosis has been observed These include: CYP2B9, CYP2B10, monoglyceride lipase, pyruvate dehydrogenase-kinase-4, cell death-inducing DNA-fragmentation factor-α, peroxisomal biogenesis factor 11β, as well as several cell recognition surface proteins including annexin A2, CD24, CD39, lymphocyte antigen 6, and retinoic acid early transcript-γ, among others. Northern blotting of total RNA extracted from the livers of PPARα-/- mice and from mice lacking both PPARα and peroxisomal fatty acyl-CoA oxidase (AOX), that were fed control and Wy-14,643-containing diets for 2 wk, as well as time course of induction following a single dose of Wy-14,643, revealed that upregulation of genes identified by microarray procedure is dependent upon peroxisome proliferation vis-a-vis PPARα. However, cell death-inducing DNA-fragmentation factor-α mRNA, which is increased in the livers of wild-type mice treated with peroxisome proliferators, was not enhanced in AOX-/- mice with spontaneous peroxisome proliferation. These observations indicate that the activation of PPARα leads to increased and decreased expression of many genes not associated with peroxisomes, and that delayed onset of enhanced expression of some genes may be the result of metabolic events occurring secondary to PPARα activation and alterations in lipid metabolism

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identification of peroxisome proliferator-activated receptor α (PPARα) target genes in mouse liver using cDNA microarray anal.)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

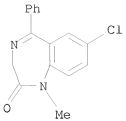
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
US 1999-165398P	P	19991105
US 2000-196571P	P	20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT 439-14-5, Diazepam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent
from gene expression profile)

RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)

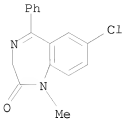


L8 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:326455 CAPLUS
DOCUMENT NUMBER: 131:208530
TITLE: A multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicology
AUTHOR(S): de Sousa, Georges; Nicolas, Florence; Placidi, Michel; Rahmani, Roger; Benicourt, Marc; Vannier, Bernard; Lorenzon, Giocondo; Mertens, Karine; Coecke, Sandra; Callaerts, Andre; Rogiers, Vera; Khan, Shamas; Roberts, Phil; Skett, Paul; Fautrel, Alain; Chesne, Christophe; Guillouzo, Andre
CORPORATE SOURCE: INSERM/Centre de Recherche Agronomique, Antibes, 06606, Fr.
SOURCE: Chemico-Biological Interactions (1999), 121(1), 77-97
CODEN: CBINA8; ISSN: 0009-2797
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ethical, economic and tech. reasons hinder regular supply of freshly isolated hepatocytes from higher mammals such as monkey for preclin. evaluation of drugs. Hence, the authors aimed at developing optimal and reproducible protocols to cryopreserve and thaw parenchymal liver cells from this major toxicol. species. Before the routine use of these protocols, the authors validated them through a multi-laboratory study. Dissociation of the whole animal liver resulted in obtaining 1-5 billion parenchymal cells with a viability of about 86%. An appropriate fraction (around 20%) of the freshly isolated cells was immediately set in primary culture and various hepato-specific tests were performed to examine their metabolic, biochem. and toxicol. functions as well as their ultrastructural characteristics. The major part of the hepatocytes was frozen and their functionality checked using the same parameters after thawing. The characterization of fresh and thawed monkey hepatocytes demonstrated the maintenance of various hepato-specific functions. Indeed, cryopreserved hepatocytes were able to survive and to function in culture as well as their fresh counterparts. The ability for synthesis (proteins, ATP, GSH) and conjugation and secretion of biliary acids was preserved after deep freeze storage. A better stability of drug metabolizing activities than in rodent hepatocytes was observed in monkey. After thawing, Phase I and Phase II activities (cytochrome P 450, ethoxycoumarin-O-deethylase, aldrin epoxidase, epoxide hydrolase, glutathione transferase, glutathione reductase and glutathione peroxidase) were well preserved. The metabolic patterns of several drugs were qual. and quant. similar before and after cryopreservation. Lastly, cytotoxicity tests suggested that the freezing/thawing steps did not change cell sensitivity to toxic compds.

IT 439-14-5, Diazepam
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism; multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicol. in relation to drug metabolism)

RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:415295 CAPLUS
DOCUMENT NUMBER: 127:130797
ORIGINAL REFERENCE NO.: 127:25089a,25092a
TITLE: In vivo induction and in vitro inhibition of hepatic cytochrome P450 activity by the benzodiazepine anticonvulsants clonazepam and diazepam
AUTHOR(S): Nims, Raymond W.; Prough, Russell A.; Jones, Collins R.; Stockus, Diana L.; Dragnev, Konstantin H.; Thomas, Paul E.; Lubet, Ronald A.
CORPORATE SOURCE: Chemistry Section, Laboratory of Comparative Carcinogenesis and Biological Carcinogenesis and Development Program, National Cancer Inst., USA
SOURCE: Drug Metabolism and Disposition (1997), 25(6), 750-756
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

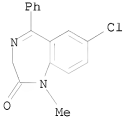
AB The ability of the benzodiazepines, as a chemical class, to cause the induction and/or inhibition of cytochromes P 450 has not been well characterized. In the present study, the induction of the cytochrome P 450 2B subfamily (CYP2B) in vivo and the inhibition of CYP2B activity in vitro by selected benzodiazepines was examined in hepatic tissues derived from male F344/NCr rats. Initial studies of the in vivo induction or in vitro inhibition of benzyloxyresorufin O-dealkylation activity revealed that both clonazepam and diazepam were relatively effective in vivo inducers of CYP2B when administered in the diet at 500 ppm for 5 days and also were fairly potent inhibitors of the activity of these hemoproteins in vitro. Oxazepam, in contrast, was ineffective as an inducer or an inhibitor of this activity. Further studies were performed to characterize the subfamily selectivity of the P 450 induction and inhibition displayed by clonazepam. Specifically, microsomes from rats treated with clonazepam (1000 or 1800 ppm in the diet for 5 days) were found to be highly induced with respect to catalytic activities mediated by CYP2B, including benzyloxyresorufin and pentoxyresorufin O-dealkylation or testosterone 16β-hydroxylation, but other CYP proteins were minimally induced. In addition to inducing the CYP2B subfamily, clonazepam also induced the RNA encoding other drug metabolizing enzymes (e.g., epoxide hydrolase and the glutathione S-transferase α-subfamily) that are typically induced by phenobarbital-type inducers. Finally, clonazepam proved to be a potent noncompetitive or "mixed-type" competitive inhibitor of catalytic activities mediated by CYP2B, but not by other CYP proteins (e.g. CYP2A, CYP3A) in microsomes

derived from phenobarbital-pretreated rats.

IT 439-14-5, Diazepam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(benzodiazepine anticonvulsants induction and inhibition of hepatic cytochrome P 450 activity)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



L8 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1996:465674 CAPLUS

DOCUMENT NUMBER: 125:161867

ORIGINAL REFERENCE NO.: 125:30167a,30170a

TITLE: Regioselectivity of Rhodococcus NCIMB 11216 epoxide hydrolase: applicability of E-values for description of enantioselectivity depends on substrate structure

AUTHOR(S): Mischitz, M.; Mirtl, C.; Saf, R.; Faber, K.

CORPORATE SOURCE: Inst. of Organic Chemistry, Graz Univ. of Technology, Graz, A-8010, Austria

SOURCE: Tetrahedron: Asymmetry (1996), 7(7), 2041-2046
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 125:161867

AB The regioselectivity of purified epoxide hydrolase from Rhodococcus NCIMB 11216 was investigated by hydrolyzing a series of structurally different epoxides 1a-5a in 18O-labeled water followed by GC/MS anal. of the 1,2-diols formed 1b-5b. The enzyme introduced a single 18O-atom in a trans-specific fashion with a varying degree of regioselectivity depending on the substitution pattern of the substrate. With an aliphatic mono-1a and 2,2-disubstituted oxirane 3a the attack occurred exclusively at the less hindered C-atom and complete retention of configuration was retained. The regioselectivity was low with a 2,3-di-4a and a trisubstituted epoxide 5a, and with a substrate bearing a benzylic oxirane atom 2a. As a consequence, the 'Enantiomeric Ratio' (E) can be applied to describe the selectivity of kinetic resolns. for some, but not for all types of substrates.

IT 75-03-6, Ethyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of epoxide hydrolase substrates and products)

RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)

L8 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1994:455036 CAPLUS
DOCUMENT NUMBER: 121:55036
ORIGINAL REFERENCE NO.: 121:9891a
TITLE: Enhanced blood pressure response to mineralocorticoid stimulation in normotensive members of hypertensive families
AUTHOR(S): Ferrari, Paolo; Travaglini, Marco; Schild, Christoph; Allemann, Yves; Shaw, Sidney; Weidmann, Peter
CORPORATE SOURCE: Med. Poliklin., Univ. Berne, Switz.
SOURCE: Blood Pressure (1992), 1(2), 86-91
CODEN: BLPREG; ISSN: 0803-7051
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Currently normotensive offspring of essential hypertensive parents often have disturbances in blood pressure (BP) regulation such as abnormalities in electrolyte homeostasis, increased salt-sensitivity and/or impaired renal Na+-excretion. Whether an altered reactivity to mineralocorticoids may also play a role is presently unknown. Therefore, the authors investigated BP (recorded during 24 h), plasma atrial natriuretic factor (ANF), cyclic guanosine monophosphate (cGMP), aldosterone (PA) and renin activity (PRA), 24-h urine electrolyte and cGMP excretions measured on 4 consecutive days, as well as other variables, after 1 wk on placebo and after 3 wk of 9α-fludrocortisoneacetate (9αF) administration, 0.6 mg/d in 12 normotensive sons of essential hypertensive parents (SEH) and 12 body-mass-index- and age-matched (25±1[±SEM]yr) sons of normotensive parents (SN). On placebo, the 2 groups did not differ significantly in average 24 h BP (mean BP 95±2 mmHg), plasma-ANF (40±7 vs 30±5 pg/mL), cGMP (6±0.4 vs 6±0.5 nmol/L), PRA (1.3±0.1 vs 1.6±0.2 ng/mL/h), PA (9±0.5 vs 10±0.9 ng/dL), hematocrit (44±0.7 vs 44±0.4%) and 96-h urinary-Na+ (mean 205±13 vs 195±16 mmol/d), -K+ (69±6 vs 78±7 mmol/d) or -cGMP (461±35 vs 483±32 nmol/d). 9αF significantly increased BP in SEH ($p<0.005$) but not SN (107±2 vs 100±2 mmHg, $p<0.05$). Elevation of BP during the night accounted for this difference (+13 vs +8 mmHg, $p<0.02$). However, during 9αF the 2 groups did not differ with regard of plasma ANF (106±13 vs 100±14 pg/mL), cGMP (10±1.1 vs 10±1.4 nmol/L), PRA (0.5±0.1 vs 0.5±0.2 ng/mL/h), PA (5±0.3 vs 4±0.3 ng/dL), 96-h urinary-Na+ (205±19 vs 195±17 mmol/d), -K+ (80±8 vs 69±6 mmol/d) or -cGMP (673±76 vs 653±62 nmol/d), plasma-Na+ (increase +3 vs +2 mmol/L), K+ (decrease -0.5 vs -0.5 mmol/L), hematocrit (42±0.8 vs 42±0.2%) or body weight (increase +2.0 vs +1.9 kg). These results indicate that normotensive offspring of hypertensive parents may react to mineralocorticoid stimulation with an enhanced BP-increase. This disturbance cannot be explained by insufficient renin-aldosterone suppression, inadequate ANF stimulation or abnormally increased Na+-fluid retention.
IT 9015-94-5, Renin, biological studies
RL: BIOL (Biological study)
(in plasma of normotensive sons from essential hypertensive families, enhanced blood pressure response to mineralocorticoid in relation to)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

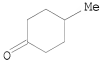
L8 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:21032 CAPLUS
DOCUMENT NUMBER: 112:21032
ORIGINAL REFERENCE NO.: 112:3695a,3698a

TITLE: Boron compounds. 87. 1,5-Cyclooctanediylboryl selenides - preparation, characterization, and application
AUTHOR(S): Koester, Roland; Seidel, Guenter; Yalpani, Mohamed
CORPORATE SOURCE: Max-Planck-Inst. Kohlenforsch., Muelheim an der Ruhr, D-4330, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1989), 122(10), 1815-24
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 112:21032
GI

I

III

AB Bis(1,5-cyclooctanediylboryl) selenide (I) is prepared quant. from bis(9-borabicyclo[3.3.1]nonane) (BBN)2 and Se in mesitylene at 150°, and the corresponding diselenide (II) is prepared by reaction of I with Se in mesitylene at 120°. I reacts with aniline to give BBN derivs. III (R = SeH, NHPh). Reactions of I with γ-picoline, Me3P, trialkoxyboranes, alkynes, Fe2O3, and other compds. are also examined, along with reactions of II and III (R = SeH).
IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cyclooctanediylboryl selenides)
RN 589-92-4 CAPLUS
CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



L8 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1977:189112 CAPLUS
DOCUMENT NUMBER: 86:189112
ORIGINAL REFERENCE NO.: 86:29653a,29656a
TITLE: The unsaturated esters of diselenophosphoric acid
AUTHOR(S): Zemlyanskii, N. L.; Mel'nik, Ya. G.; Turkevich, V. V.; Makota, I. P.; Koretskii, A. S.
CORPORATE SOURCE: USSR
SOURCE: Visnik L'vivs'kogo Derzhavnogo Universitetu, Seriya Khimichna (1975), 17, 65-8
CODEN: VLDUAB; ISSN: 0460-0509
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian
AB (RO)2P(Se)SeH (R = Et, Pr, Me2CH, Bu) were neutralized with K2CO3 and then treated with R1Br (R1 = allyl, HC.tplbond.CCH2) in Me2CO at 40° to give 71-82% (RO)2P(Se)SeR1 (I). Mol. association was deduced

from the IR spectra of all 4 I (R1 = CH2C.tplbond.CH).
IT 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of dialkyl diselenophosphates with)
RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)

L8 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1938:63839 CAPLUS
DOCUMENT NUMBER: 32:63839
ORIGINAL REFERENCE NO.: 32:8937i,8938a
TITLE: Raman effect. LXXXVI. Ethyl derivatives
AUTHOR(S): Wagner, J.
SOURCE: Z. physik. Chem. (1938), B40, 439-49
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 32, 6549.5. Raman spectra were obtained for EtX, where X = OH, SH, Cl and I. Results of other investigations, where X = Me, NH2, Br and SeH have been included in the calcns. The mols. have been treated as a 3-particle system with a valence force potential energy function. The calculated vibrational frequencies agree with experiment only if the atomic weight of
X is less than 36. The valence force consts. are smaller and the nuclear distances are larger than those for the corresponding methyl derivs.
IT 75-03-6, Ethane, iodo-
(Raman spectrum of)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

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